Quality of Life and Depression in patients with Primary Open Angle Glaucoma using Malay version of Glaucoma Quality of Life 36 and Malay version Geriatric Depression Scale 14 questionnaires

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DISCLAIMER

I hereby certify that the work in this dissertation is my own except for the quotations and summaries which have been duly acknowledged. I declare that I have no financial interest in the instruments in this study.

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TABLE OF CONTENTS **Page**

CHAPTER 2: OBJECTIVE

CHAPTER 3: METHODOLOGY

LIST OF TABLES **Page**

LIST OF FIGURES **Page**

ABBREVIATIONS

POAG	Primary open angle glaucoma
GlauQoL 36	Glaucoma quality of life 36
mGDS 14	Malay version geriatric depression scale 14
GDS	Geriatric depression scale
MMSE	Mini mental state examination
IOP	Intraocular pressure
SIP	Sickness impact profile
SF 36	Short form health survey 36
CIGTS	Collaborative Initial Glaucoma Study
VF 14	Visual function 14
NEIVFQ	National Eye Institute Visual Function Questionnaire
GSS	Glaucoma Symptoms Scale
GQL 15	Glaucoma Quality of Life 15
QoL	Quality of life
mLOCS II	Modified Lens Opacities Classification System II

ABSTRAK

PENDAHULUAN

Glaukoma adalah penyakit kronik yang memerlukan rawatan sepanjang hidup. Kualiti hidup pesakit glaukoma kerap tidak dititikberatkan dalam rawatan penyakit tersebut. Pemahaman mengenai kualiti hidup dan saringan awal kemurungan pesakit glaukoma primer membantu dalam rawatan penyakit. Di Malaysia, masih terdapat jurang dalam pemahaman mengenai kualiti hidup dan kemurungan di antara pesakit geriatrik glaukoma primer.

OBJEKTIF

Menilai kualiti hidup dan kemurungan di antara pesakit glaucoma primer dengan menggunakan borang soal selidik skala glaucoma QoL 36 (GlauQoL 36) dan skala kemurungan geriatric 14 (mGDS 14). Kajian ini juga cuba untuk mengaitkan kualiti hidup dan kemurungan dengan tahap glaukoma. Korelasi antara kualiti hidup dan kemurungan juga di kaji.

METODOLOGI

Suatu kajian keratan rentas bandingan telah dijalankan di Hospital Universiti Sains Malaysia, Kelantan dan Hospital Selayang, Selangor di antara Julai 2014 dan Februari 2016. Pesakit POAG yang melebihi 60 tahun pada waktu kajian telah direkrut. Pesakit mempunyai mLOCS II gred 1 atau kurang, menjalani pembedahan trabeculektomi atau katarak sekurang kurangnya 3 bulan sebelum kajian dan sedang mengambil rawatan untuk glaukoma primer. Tahap glaukoma primer adalah berdasarkan 'Advanced Glaucoma Intervention Study' (AGIS) menggunakan dua analisis medan penglihatan Humphrey SITA program 24-2 yang dipercayai. Temuduga bersemuka dijalankan menggunakan borang soal selidik GlauQoL 36 dan mGDS 14 yang telah divalidasi.

KEPUTUSAN

Seramai 360 pesakit telah menyertai kajian ini. Kebanyakan pesakit di antara umur 60-69 (38.3%). Secara keseluruhan, 64 (17.8%) menghidapi glaucoma ringan, 93 (25.8%) menghidapi glaucoma sederhana, 115 (31.9%) menghidapi glaucoma teruk dan 88 (24.4%) menghidapi glaucoma peringkat akhir. Kebanyakan pesakit tidak berkerja (88.9%) dan tinggal bersama keluarga (68.1%). Perbezaan statistik signifikasi diperolehi di antara semua domain borang soal selidik GlauQoL 36 dan tahap glaukoma primer: kehidupan seharian, memandu, jiwa, imej diri, kebimbangan, halangan dan sokongan. Kualiti kehidupan menurun apabila tahap glaucoma primer semakin naik dalam semua domain kecuali domain sokongan. Terdapat lebih ramai pesakit dengan kemurungan apabila tahap glaukoma meningkat. Korelasi yang lemah diperolehi di antara kualiti hidup dan kemurungan di antara kumpulan POAG ($r < 0.25$).

KESIMPULAN

Versi Bahasa Malaysia GlauQoL 36 dan mGDS 14 adalah alat yang berguna dalam mengkaji kualiti hidup dan kemurungan pesakit POAG di Malaysia. Kualiti hidup berkurangan apabila tahap glaukoma semakin meningkat. Kemurungan adalah lebih tinggi dalam tahap glaukoma teruk. Bagaimanapun, korelasi lemah diperolehi di antara kualiti hidup dan kemurungan.

ABSTRACT

INTRODUCTION

Glaucoma is a chronic disease requiring life long treatment. Quality of life (QoL) is often under emphasized during the course of glaucoma management. Understanding the quality of life and detection of early depression at different severity stage of POAG not only helps in coping with the disease but also in customization of the management. There is still a wide gap in understanding the QoL and depression in elderly with POAG in Malaysia.

OBJECTIVE

To evaluate quality of life and depression in patients with primary open angle glaucoma using the Malay version of the Glaucoma Quality of Life- 36 (Glau-QoL 36) and malay version Geriatric Depression Scale 14 (mGDS 14) questionnaires. This study also aims to compare the QoL and depression with severity of POAG. The potential correlation between QoL and depression was also studied.

METHODS

A cross sectional study was conducted in Hospital Universiti Sains Malaysia, Kelantan and Hospital Selayang, Selangor between July 2014 and February 2016. POAG patients who were ≥ 60 years old at the time of recruitment had mLOCS II grade 1 or less, underwent cataract or trabeculectomy surgery at least 3 months prior and were on medical or combined medical and surgical treatment. Severity of POAG was based on modified Advanced Glaucoma Intervention Study (AGIS) based on two reliable reproducible Humphrey visual field SITA program 24-2 analysis. Face to face interview was conducted using validated Bahasa Malaysia version of GlauQol 36 and mGDS 14 questionnaires.

RESULTS

A total of 360 patients were recruited. Majority of recruited patients were between ages 60-67 (38.3%). Overall 64 (17.8%) have mild POAG, 93 (25.8%) have moderate POAG, 115 (31.9%) have severe POAG and 88 (24.4%) have end stage POAG. Majority of the recruited patients were not working (88.9%) and live with their families (68.1%). There was significant association between GlauQoL 36 score among POAG patients according to severity and domains: daily living, driving, physiological well being, self image, anxiety, burden of treatment and confidence in healthcare. Increased severity of POAG was associated with dectresed quality of life in all GlauQoL 36 domains except confidence in healthcare. There were more depressive patients as severity of POAG increased. There was poor correlation between quality of life and depression among POAG patients (r <0.25).

CONCLUSION

Bahasa Malaysia version of GlauQoL 36 and mGDS 14 is a useful tool to assess QoL and depression of POAG patients in Malaysia. GlauQoL 36 scores increased as the severity of glaucoma increases suggestive of poorer quality of life. The mGDS 14 score also increases as the severity of glaucoma increases. However, there was poor correlation between QoL and depression based on the mGDS 14 and GlauQoL 36 questionnaire.

GLAUCOMA

Glaucoma is a group of disease that causes progressive damage to the optic nerve, which left untreated gradually progresses to visual damage and may lead to blindness (World Glaucoma Association, 2015).

However, from the early 1880's until last quarter of the 20th century, glaucoma was defined as 'pressure within the eye higher than the statistical normal of the population' (Von Graefe A & Windsor T, 1859; Keyser PD, 1864). This concept as a defining characteristic for glaucoma has been almost universally discarded. This is based on studies documenting disc and field damage in people with statistically normal intraocular pressure (Foster & Quigley, 2002).

Glaucoma is the second most common cause of blindness in the world with nearly 66 million people suffering from this chronic ophthalmologic condition (Weinreb RN & Khaw PT, 2004; Quigley HA & Broman AT, 2006). It is projected to become the most common cause of blindness worldwide (Vanderbroeck S et al, 2011). The number with open angle glaucoma in 2010 was highest among European population (23.9%) compared to Asians (4.7%) (Quigley HA & Broman AT, 2006). It has been projected that by 2020 the number of open angle glaucoma patients in Asian regions will increase to 5.2%; an increase of 1 million people (Quigley HA & Broman AT, 2006). The global glaucoma blindness is estimated to be 5.2 million people (15%) (Thylefors B & Negrel A-D, 1994). Blindness in the European population ranged from 2.5 to 8% whereas in African Americans it was 8.0% (Thylefors B et al, 1992). A study conducted in Singapore documented the rate of uniocular blindness from

POAG to be 27% and PACG 50% while binocular blindness is 9% for POAG and 29% for PACG (Foster PJ et al, 2000).

Glaucoma can be classified into 2 broad groups based on the angle structures; open and closed angle glaucoma. This can be further subdivided into primary and secondary glaucoma (Quigley HA, 1996). The prevalence of each type of glaucoma varies according to the region with open angle glaucoma having an equal distribution while closed angle closure glaucoma is more prevalent in Asia (Quigley HA, 1996).

Glaucoma often requires lifelong treatment and carries a risk of serious visual impairment. Patients' may experience progressive worsening of their vision, initially peripherally but eventually involving the central vision (Khadka J et al, 2013). Advancing age is strongly correlated with the progression of glaucoma to blindness in both eyes as well as in at least one eye (Hattenhauer et al, 1998; Jacob A et al, 1998; Dandona L et al, 2000). It has been estimated that a probability of 9% for bilateral blindness and a 27% for unilateral blindness in open angle glaucoma patients (Hattenhauer et al, 1998).

Traditionally, evaluation of outcomes in glaucoma clinical trials has focused on clinical measures of glaucoma status, mainly the extent of visual field loss and level of intraocular pressure measurement. However, such measures do not capture the effects of glaucoma or its treatment on activity limitation and wellbeing (Che Hamzah J et al, 2011). The effects of glaucoma on well being are better assessed by outcomes reported by glaucoma patients in the form of questionnaires as it is able to capture the effect of glaucoma on their daily living.

1.1 PRIMARY OPEN ANGLE GLAUCOMA

POAG is characterized as a chronic, slowly progressive visual field loss and optic nerve cupping, often associated with an elevated IOP with visually open anterior chamber angles by gonioscopy, without underlying secondary ocular disease (European Glaucoma Society, 2014).

Glaucoma is a disease of longevity. Advancing age is a risk factor for POAG (Jacob A et al, 1998; Ramakrishnan R et al, 2003; Leske MC et al, 2001). The mean age of developing glaucoma is 68.1 (4.9 SD) years (Leske MC et al, 1999). Due to improvement of life expectancy and healthcare, the number of people with glaucoma is expected to rise; which poses a substantial public health challenge worldwide (Ying P and Varma, 2011). Increasing age is known to increase the risk of developing glaucoma in individuals with elevated intraocular pressure and for progression of glaucoma (Leske MC et al, 2007; Gordon MO et al, 2002; European Glaucoma Prevention Study Group, 2007). The hazards ratio is 1.32 per decade (95% CI; 1.17, 1.71) (European Glaucoma Prevention Study Group, 2007). In the Early Manifest Glaucoma Trial, faster and greater progression was noted in older patients (> 68 years of age) when compared to younger patients (Leske MC et al, 1999).

Barbados Eye Study found an increase of 2.5 times from 1.2% at ages 40-49 to 4.2% at the age of 70 and above (Leske MC et al, 2001). The Kandy Eye Study found that in Sri Lanka patients 70 years and above were six times more likely to develop POAG as compared to those in their fourth decade (p=0.003) (Sia DI et al, 2010). In a study

conducted in Japan, older age groups had OR of 1.06 (95% CI; 1.04, 1.08) to develop POAG (Suzuki Y et al, 2006).

Although glaucoma encompasses a diverse group of disease, its hallmark include progressive irreversible damage to the optic nerve head and the retinal ganglion cells with corresponding visual field loss (Tuulonen A and Airaksinen PJ, 1991). This results in progressive and asymmetric changes in the optic cup, with corresponding visual field loss. Typically, structural changes occur before functional loss (Tuulonen A and Airaksinen PJ, 1991).

The cardinal features of open angle glaucoma at the optic disc are a reduction in neuroretinal rim area and enlargement of the optic cup; both of which are related to the age of the individual (Garway-Heath D F et al, 1997). A number of histological studies have found an age related decline in optic nerve axon count, with an estimated rate of decline around 0.36% to 0.62% per year (Balazsi AG et al, 1984; Johnson BM et al, 1987; Jonas JB et al, 1990). Faster progression was also noted if disc hemorrhages and greater visual field loss was noted at the initial presentation (Leske MC et al, 1998).

The impact of glaucoma on quality of life (QoL) is substantial and early recognition and treatment is important. Preventing vision loss from glaucoma means that secondary medical problems from falls or developing depression are avoided and independence maintained (Bramley et al, 2008). There is a 58.6% risk of falls and accidents due to vision imparment (Bramley et al, 2008). Glaucoma also increases the

risk for hip fracture by 2.6 times which was almost comparable to osteoporosis (Colon-Emeric CS et al, 2003).

1.2 QUALITY OF LIFE

The term "quality of life" is defined by the World Health Organization as individuals' perception of their position in life in the context of culture and value systems in which they live in relation to their goals, expectations, standards and concerns (World Health Group, 1995). It is a broad ranging concept, incorporating individuals' physical health, psychological state, level of independence, social relationships, and their relationship with their environment (Felce D, 1995).

QoL is multidimensional and is assessed based on an individuals' perception (Xavier MF et al, 2003; Bechetoille A et al, 2008). Currently, it is agreed that QoL is a hierarchical model with three levels (Spilker B, 1990; Schiffer H, 1990; Janz et al, 2001; Patrick DL and Deyo DA, 1989). The first level is the overall assessment of QoL as proposed by the World Health Organization. The second level comprises three main domains: functional, psychological and social functioning. The third level corresponds to specific aspects of each of these domains (i.e anxiety or depression specific to the psychological domain (Spilker B, 1990; Schiffer H, 1990; Janz et al, 2001; Patrick DL and Deyo DA, 1989).

QoL has health economic implications and knowledge of its impact, will help determine at which level screening of the diesease will outweigh its cost (Hernandez

RA et al, 2008). The main characteristic determining QoL in the elderly is resilience; which is the emotional capability of recovering from stressing factors (Rowe JW & Khan RL, 1997). The task of recovering from stress factors is hampered if they sustain too many emotional or psychological stressors at the same time (Sadavoy et al, 1995). QoL varies between individuals'; however the common denominator for poor QoL is health (Xavier MF et al, 2003).

There are two ways to measure QoL: through structured and non structured interviews. The structured instruments use scales of 0 - 5 to measure QoL comprising of very positive, positive, neutral, negative and very negative whereas non structured interviews allows individuals to identify the factors which contribute for their positive or negative attribution to the QoL (Farquhar M, 1995).

1.2.1 GLAUCOMA AND QUALITY OF LIFE

Glaucoma affects daily life through visual deterioration and the treatment (Lester M & Zingrian M, 2002). Patients with glaucoma may experience diminished QoL for several reasons; understanding of diagnosis, fear of functional loss, inconvenience of treatment, side effects of treatment and cost of treatment (Lester M & Zingrian M, 2002). Though limitations of disease may only affect patients toward the later stages of disease, it has been noted that QoL can be affected even at early stages of the disease (Khadka J et al, 2013; Xavier MF et al, 2011; Lamoureux EL et al,2011).

Studies have found a relationship between visual field loss and declining QoL (Gutierrez et al, 1997; Mills RP, 1998; Parrish RK, 1997; Jampel HD, 2001). Adjusted mean scores for QoL scores were lower for patients with glaucomatous visual field loss, compared to patients without visual field loss (Gutierrez et al, 1997; Freeman EE et al, 2006). Patients with glaucomatous visual field loss had the greatest difficulty with driving activities (Freeman EE et al, 2006, Parrish RK, 1997; Gutierrez et al, 1997;). This could be due to limitations in glare and dark adaptations which exaggerate the visual field loss (Dengler-Harles M et al, 1990).

It has also been found that patients with the same degree of mean deviation in visual field loss may have different location of the visual filed defect thus having a different effect on QoL (Murato H et al, 2013; Sawada H et al, 2014). Central visual field defects in the better eye negatively affects QoL as they affect activities like facial recognition, finding objects, reading signs (Sawada H et al, 2014; Van Gestel A et al, 2010; Henderer J et al, 2009; Okomoto M et al, 2014). Inferior visual fields were associated with poorer QoL as they affect activities like walking down the stairs (Sun Y et al, 2015; Black A eta al, 2011; Sawada H et al, 2014; Sumi I et al, 2003). However another study found that superior hemifield defects are associated with near activity difficulties (ChangHC et al, 2014). Therefore, early treatment is necessary to prevent loss of QoL.

Vision loss from glaucoma causes patients to have difficulty in all aspects of daily living including driving, walking, preparing meals, doing housework, reading; mental health including social withdrawal and depression; side effects of treatment and fear from blindness (Cardarelli WJ et al, 2013; Ramulu PY, 2009; Skalicky S et al, 2008;

Perfetti S et al, 1998; Bournias TE et al, 2004). Based on a cross sectional study, glaucoma patients had a significantly higher risk of prevalence of impaired QoL (OR: 2.20; 95% CI: 1.31, 3.70) as compared to healthy subjects (Park et al, 2015). Glaucoma patients also had a significantly higher risk of impaired activity of daily living (OR 2.06; 95% CI:1.14, 3.71) as compared to healthy subjects (Park et al, 2015).

A cross sectional study comparing walking in patients with and without glaucoma demonstrated bilateral glaucoma walked 0.04m/second slower ($p<0.05$) (Friedman DS et al, 2006). However similar findings were not found in unilateral glaucoma as bilateral glaucoma missed more points on visual field than did unilateral glaucoma (Friedman DS et al, 2006). Another aspect of QoL that is affected is near and central vision tasks i.e reading. It was noted that 43% of glaucoma patients complained of difficulty reading (Nelson P et al,1999). Patients with bilateral glaucoma read 29 words/min slower than those without glaucoma ($p<0.001$) (Ramulu PY et al, 2008). It was also noted that bilateral advanced glaucoma patients reading speed was 32 words/min slower than subjects without glaucoma (95% CI: -56,-7) (Ramulu PY et al, 2008). Older patients with distant and near vision loss are more dependent on others for daily living activities, are less likely to partake in social and recreational activities and more likely to have mobility disorders and falls due to the loss in balance associated with visual disturbance (Lamoureux EL et al, 2009; Meada A et al, 1998; Nakamura T et al, 1998).

QoL in patients with reduced vision were higher in individuals with lower education and no occupation (Nirmalan PK et al, 2005). Patients without any formal education

seemed to encounter significant difficulty in performing fine work ($p = 0.005$) and doing outdoor activities ($p = 0.019$) (Maharajah KR et al, 2008). Those who underwent surgery for glaucoma had poorer QoL (Gupta V et al, 2005). The association of systemic disease with reduction in QoL scores was found to be not significant (Gupta V et al, 2005; Hyman LG et al, 2004). Another study however, found the statistical significance between systemic disease and QoL scores (Lin JC and Yang MC, 2008).

The number of glaucoma medications and the number of applications is associated with poorer QoL (Balkrishnan R et al, 2003; Montmeyor F et al, 2000; Sherwood MB et al, 1998). However there have been studies where the number of glaucoma medications was not predictive of QoL (Rossi GCM et al, 2010; Wilson MR et al, 1998).

Fear of blindness was was also noted to be associated with poorer QoL (Odberg T et al, 2001; Janz NK et al, 2007). 34% reported a moderate or a lot of worry to going blind at baseline that decreased to 11% over a period of 5 years. Despite the decreasing trend, 50% remained slightly worried after 5 years (Janz NK et al, 2007). The reduction in fear is due to multiple factors such as reassurance, more knowledge and acceptance of the diagnosis (Odberg T et al, 2001; Janz NK et al, 2007).

1.2.2 HEALTH RELATED QUALITY OF LIFE

Health related quality of life (HRQoL) refers to a person's self perceived functioning and well being (Schipper H, 1990). HRQoL restricts the concept of QoL to aspects specifically related to health (Schipper H, 1990). HRQoL is an important expansion to the normal traditional methods of assessing disease in the form of symptoms, signs and morbidity (Konrad Pseudovs et al, 2010). It is a holistic approach to assess the impact of disease on patients physical, social and emotional well being. It is increasingly used to measure the effects of chronic illness on an individual's daily life and is regarded as the ultimate goal of all health interventions (Rubin RR & Peyrot M, 1999). HRQoL is a valid health indicator in evaluating diseases and is routinely asessed through questionnaires (Zakaria ZF et al, 2009). Evidences suggest that assessment of this parameter improves care on multiple levels such as improvement in patient communication and problem identification (German PS et al, 1987; Zung WW et al, 1983; Detmar SB et al, 2002). This results in improved patient satisfaction (Wasson JH et al, 1999).

Traditionally, clinicians are trained to obtain the qualitative aspects of medical history such as vital signs but not the quantitative measurement such as HRQoL (Hahn E et al, 2007). Patients perception of well being is often discordant with the assessment by clinicians (Hahn E et al, 2007). Assessment of HRQoL improves clinical practice through detection of psychological problems, monitoring disease and treatment and altering of treatment plans when needed (Greenhalgh J et al, 1999; Espallargues M et al, 2000; Lohr KN, 1992; Till JE, 1994).

1.3 PATIENT REPORTED OUTCOMES

Patient reported outcomes are defined as 'outcomes reported by patients' (Bradley C, 2006). It measures any aspect of the patients health reported by the patient, free of bias from any other person (Varma R et al, 2010). The European Committee for medicinal products for human use defines patient reported outcomes as patient's perception of a disease scored by the patient himself (Mapi Research Trust, 2009). It complements objective clinical measurements and is able to assess the effectiveness of treament.

Objective assessment of vision loss may not capture the overall impact of glaucoma on the subject's daily life (Hartmann CW et al, 2006). In a cross sectional study, comparing a group of visual function tests, including near visual field, contrast sensitivity and superimposed monocular kinetic visual field, in a 84-item questionnaire; found that the psychophysical tests were the best predictors of the perceived disability (Ross JE et al, 1984).

Patient reported outcomes can be on general health, vision specific or disease specific (Varma R et al, 2010; Spaeth G et al, 2006). General health related questionnaires such as Sickness Impact Profile (SIP) and Short Form Health Survey 36 (SF 36) serves to identify general health related domains.

SF 36 was developed in 1992 by Ware and Sherbourne for use in clinical and research practice. It is able to assess patients physical and mental status. It was designed to be versatile and be used in a variety of diseases (Mapes et al, 2003; Patti et al, 2003;

Strassnig et al, 2003). It contains 8 domains (physical functioning, physical role limitation, emotional role limitation, social functioning, bodily pain, mental health, vitality and general health) and consists of closed ended questions (Wares et al, 1992). Validity and reliability studies showed that the questionnaire could be used across a variety of patients (Mc Horney CA et al, 1993; Mc Horney CA et al, 1994). However, when SF 36 was administered to patients with glaucoma there was weak correlation between the SF 36 scores and visual field loss (Parrish RK et al, 1997; Jampel HD et al, 2002). Therefore, it was difficult to attribute reduced SF 36 scores to effects of glaucoma compared to other health conditions that might concurrently be present (Spaeth G et al, 2006).

Sickness Impact Profile (SIP) is another general health related questionnaire. It consists of 136 item questionnaire divided into 12 categories (body care and movement, mobility, ambulation, emotional behaviour, social interaction, alertness, communication, sleep and rest, home management, work, recreation and pastimes and eating) (Pollard WE et al, 1976; Bergner M et al, 1981). It contains two dimension scores (physical health and psychosocial) and can be used across a variety of patients (Pollard WE et al, 1976; Bergner M et al, 1981; De Bruin AF et al, 1992). A modified SIP has been used in the Collaborative Initial Glaucoma Treatment Study (CIGTS) correlated significantly with health status (Janz NK et al, 2001). However, it takes 20-30 mins to administer the questionnaire which causes considerable effort to the elderly. The use of proxy respondants such as family members showed poor correlation between SIP and the patients' scores which does not truly reflect the patients QoL (Gilson BS et al, 1980; McCusker J et al, 1984; Goldsmith G et al, 1989).

Vision specific questionnaire such as Visual Function Index 14 (VF 14) and National Eye Institute Visual Function Questionnaire (NEIVFQ) measures effect of vision problems on activities of daily living (Yu Q et al, 1996; Mangione CM et al, 1998; Keefe JE et al, 1999). It is more specific than general health questionnaires.

VF 14 questionnaire was developed to assess effect of cataract on vision related activities (Steinberg EP et al, 1995). It comprises of 14 questions encompassing 14 vision related activities such as reading small print, doing fine work, night driving, daytime driving, reading newspaper, reading signs, writing checks, watching television (Steinberg et al, 1994). Administration of VF 14 questionnaire to glaucoma patients showed a weak to moderate correlation between the score and visual field loss (Parrish RK et al, 1997; Jampel HD et al, 2002; NahYS et al, 2000; Guttierez P et al,1997). VF 14 comprises of daily living and driving activites but does not include psychosocial assessment and burden of treatment which also contributes to QoL of glaucoma patients.

NEIVFQ is another vision specific questionnaire that measures vision dependent function and QoL in a variety of ocular conditions (Mangione CM, Berry S et al, 1998). It comprises of 51 questions grouped into 8 function based categories (general vision related concerns, mobiity, reading, social relations and activities, home activities, self care activities and personal finances) (Mangione CM, Berry S et al, 1998). Administration of NEIVFQ questionnaire to glaucoma patients showed a moderate correlation wih visual field loss (Mangione CM, Lee PP et al, 1998; Parrish RK et al, 1997; Guttierez P et al, 1997). However, it does not correlate well with

symptoms of glaucoma when NEIVFQ was compared to a glaucoma specific questionnaire; the Glaucoma Symptom Scale (Lee BL et al, 1998).

Glaucoma specific instruments such as the Glaucoma Symptom Scale (GSS) and Glaucoma Quality of Life 15 (GQL 15) were developed specifically to assess visual field loss with QoL in glaucoma patients (Spaeth G et al, 2006). GSS contains 10 items with regards to symptoms of glaucoma divided into nonvisual symptom subscale (burning/stinging, tearing, dryness, itching, soreness and foreign body sensation) and visual subscale (blurry/dim vision, difficulty seeing in daylight, difficulty seeing in darkness, halos around light) (Lee BL et al, 1998). GSS scores was able to discriminate between patients with and without glaucoma (Lee BL et al, 1998). Visual acuity had modest correlation with GSS scores but did not demonstrate association with binocular visual field changes (Noe G et al, 2003). GSS measures only the symptom aspect of glaucoma patients. Limitation of daily activity, burden of treatment and psychosocial aspect are not assessed which also contributes to glaucoma patients QoL (Khadka J et al, 2013).

GQL 15 is another glaucoma specific instrument. It was developed by choosing questions that correlate best with visual field loss (Nelson P et al, 1999). It consists of 15 questions divided into glare factor, peripheral vision factor, central/near vision factor and outdoor mobility factor (Nelson P et al, 1999). GQL 15 was able to detect decreased visual ability even in mild visual field loss (Nelson P et al, 2003). However, GQL does not truly assess QoL; which is a multidimensional concept as it contains only questions regarding visual activities (Nelson P et al, 1999; Nelson P et al, 2003) and not the psychosocial components.

Administering questionnaires in elderly people need to be done through a conversational approach (De Vries K et al, 2014). The use of closed questions and adherence to questionaire protocol were barriers to communication with older people as they seldom express their concerns and emotions directly. The data validity obtained when using strict close ended questions is undermined (Isaksson U et al, 2007; Suchman L et al, 1990). Therefore, administrating questionnaire to the elderly needs to be done in an engaged conversational manner to avoid missing cues (Suchman L et al, 1990).

1.4.1 GLAUCOMA QUALITY OF LIFE 36

The Glaucoma Quality of Life 36 (GlauQoL 36) questionnaire is the first available health related QoL tool specific to glaucoma that covers all stages of the disease (Bechetoille A et al, 2008). It comprises of 36 items, covering seven health related QoL domains relevant to glaucoma; physiological well being, self image, daily life, burden of treatment, driving, anxiety and confidence in health care (Bechetoille A et al, 2008).

The initial pilot questionnaire contained 151 items covering all aspects of HRQoL and was written in French (Rouland el al, 2002). Questions that were misunderstood by patients or unclear were eliminated leaving 36 questions (Rouland el al, 2002; Juniper et al,1996). Responses by patients were ranked on a 4- or 5- mode scale and scored by summing each domain (Rouland el al, 2002). The construct validity (i.e analysis to assess if the questionnaire measures what it was intended to) is satisfactory

(correlation coefficent >0.40) as different domains of the questionnaire assesses a specific aspect of QoL (Campbell et al, 1959; Bechetoille A et al, 2008). The questionnaire was able to assess the QoL at different severities of glaucoma as well as different levels of visual field loss (Bechetoille A et al, 2008; Rouland el al, 2002).

Advantages of GlauQoL 36 compared to existing HRQoL questionnaires such as VF 14, NEIVFQ and GQL 15 is that, it not only covers aspects related to daily functioning but also on burden of treatment, mental health and self image. This allows the questionnaire to be also used in ocular hypertensive patients and glaucoma patients that do not have problems in function yet (Sloane et al,1992; Steinberg et al, 1994; Nordmann et al, 2004; Nelson et al, 2003).

To date, this questionnaire has been used in a French study in 2002 (Rouland el al, 2002) and its translated Malay version in a study in 2015 (Chandramohan H et al, 2015). However the translated Malay version assessed all glaucoma patients including POAG and PACG. There are no known studies in English that have used GlauQoL 36 in assessing the QoL in glaucoma patients. The translated version of this questionnaire in malay language will be the first to assess the QoL in POAG patients in the Malaysian setting.

1.4 DEPRESSION

Depression is a broad and heterogeneous diagnosis. Depression is defined as a feeling of depressed mood or loss of interest with at least five out of nine symptoms present for a diagnosis of major depression (DSM IV; American Psychiatric Association 2000). Symptoms should be present for at least 2 weeks and each symptom should be present at sufficient severity for most of the day. The key symptoms include low mood, loss of interest and pleasure or loss of energy (DSM IV; American Psychiatric Association 2000). A depressive episode may be either idiopathic or secondary to another medical condition or drug (DSM IV; American Psychiatric Association 2000). Both the number, severity of symptoms and degree of functional impairment determine its severity.

Depression is projected to be the second leading cause of disability worldwide by 2020 (Murray CJ et al, 1997). The World Health Organization estimates that depression will be a major burden of illness in most developing countries (World Health Organization Depression, 2011). The prevalence of depression range from 4.8% in Spain to 35% in Turkey (Lobo A et al, 1995; Bekaroglu et al, 1991). The prevalence of depression in the Asia-Pacific Region which ranged from 1.7 to 6.7% is comparable to that of the Western world (Chiu E et al, 2004). Depression affects females twice as more than males (Depression Facts and Statistics, 2011). Depression is the most common mental illness reported in Malaysia (Mukhtar F & Tian PS, 2011). Overall prevalence in Malaysia range between 3.9% to 46% (Kit et al, 1997; Kadir et al, 2005; Saniah et al, 2010).

Risk factors for depression include gender, level of education, health, functional and degree of social support (Blazer DG, 2002; Bruce ML, 2002; Izzuna NMG et al, 2006). Marriage is known to be a protective factor for depression due to presence of companionship (Chen RL et al, 2008; Blay SL et al, 2007; Winrow AM et al, 2005). Depression in turn causes increased morbidity, stroke and heart failure (Mitchell AJ et al, 2005; Jonas BS et al, 2000; Ohira T et al, 2001; Ariyo et al; 2000).

In the elderly population, disability is a known risk factor for depression (Simon Skalicky et al, 2008). Depression causes functional impairment and imposes a burden on individuals, communities and health services (Rashid A et al, 2010).

1.4.1 DEPRESSION IN GERIATRICS

The United Nations and Malaysian ministry of health defines the elderly or ageing population as individuals aged 60 years and older (Health of the Elderly, WHO 1989; Jalal BH, 1995). It is defined as a biological, sociological, economic and chronological phenomenon (Karim HA, 1997). Worldwide, it is projected that the elderly population will rise by 21% in the next 50 years; and by 2050 there will be an expected quadruple increase in elderly population to almost two billion in the developing countries (Venne R, 2005).

The proportion of older people among the Malaysian population is estimated to increase from 6.2% in 1990 to 11.3% by 2020 due to increased life expectancy, low mortality, declining fertility and a healthier living environment (Arokiasamy JT,

2000). Based on the past four national censuses in Malaysia (1970, 1980, 1991 and 2000); the proportion of younger age is decreasing, while the proportion of older people is on the rise (Ong, 2001) leading to inversion of the base of the pyramid. The population of the elderly is the highest in northwest Malaysia (Rashid AK et al, 2006). Increase of an aged population, results in increase number of chronic and non communicable diseases including mental health such as depression (Omran AR, 1971).

A metaanalysis study revealed worldwide prevalence of depression in the elderly to be 4.6 to 11% (Barua et al, 2011). In US and European countries depression in the elderly range from 0.9% to 49% (Djernes, 2006; Blazer, 2003). In Malaysia, prevalence of depression among the elderly range from 14% to 18% (Norsiah MN, 1999; Sherina MS, 2002).

In a cross sectional study done in Malaysia, the prevalence of depression among elderly was 30.1% with mild depression and 9% with severe depression (Rashid A et al, 2010). In the same study, more females have depression (32%) compared to males (27.7%) (Rashid A et al, 2010). The gender difference was similar to other studies worldwide (Alexopoulos GS , 2005; Djernes JK, 2006).

Physical health was found to be the most important factor associated with depression (Li N et al, 2016; Alexopoulos GS , 2005; Djernes JK, 2006; Cole and Dendukuri, 2003). The other risk factors associated with depression are living arrangements, sleep disturbances, total income and bereavement (Imran A et al, 2009; Cole and Dendukuri, 2003; Li N et al, 2016).

In addition, depression increases mortaliy and morbidity in the elderly (Mitchell AJ & Subramaniam H, 2005). Suicide is twice as frequent in elderly as in general population (Alexopoulos GS et al, 2002). Depression is associated with increased risk of stroke, heart failure and hospitalization (Ariyo AA et al, 2000). Therefore, early detection and successful treatment of depression is essential.

It is difficult to diagnose depression in the elderly. The presence of multiple medical problems and cognitive impairment complicate the diagnosis (Imran A, et al, 2009; Kahn et al, 1975). Memory loss and cognitive impairment in the elderly (Kahn et al, 1975) are less frequently seen in younger individuals (Yesavage JA & Brink TL, 1981). Conversely, somatic symptoms which are a key to diagnosis of depression in the young are less useful in the elderly as they tend to have multiple medical problems (Yesavage JA & Brink TL, 1981). Due to the presence of cognitive impairment and high prevalence of somatic symptoms, screening tool for depression needs to be easily understood, minimizes on somatic components while concentrating on the psychological aspects of depression.

1.4.2 DEPRESSION AND GLAUCOMA

It has been found that a third of individuals with vision impairment report clinically significant depressive symptoms (Rees G et al, 2010). Prevalence of depression among glaucoma patients ranges between 9 – 30% (Wang SY et al, 2012, Jayawant SS et al, 2007; Mabuchi F et al, 2008; Yochim BP, 2012). In glaucoma patients, the disease process, fear of future vision loss and potential side effects of treatment

contributes to depression (Jampel HD et al, 2007; Wilson MR et al, 2002). There is increased depression with increased severity of glaucoma in individuals in their 70s (Skalicky S et al, 2008).

Studies on association of depression in glaucoma have conflicting findings. Cumurcu et al found a higher rate of depression among patients aged 30 to 80 years with psedoexfoliative glaucoma compared with controls. Mabuchi et al (2008) focused on older glaucoma patients with a mean of 64 years (SD:12.1) and found a prevalence of 10.9%. Yochim et al (2012) found a prevalence rate of 12.2% in glaucoma patients compared to control. Wilson et al (2002) assessed depression among mild glaucoma and controls and found the prevalence to be equivalent. Erb et al (1999) also found no difference in depression between normal tension glaucoma and control groups.

Depression can occur regardless of the level of vision impairment (Wang ST et al, 2012). Objective measurements of glaucoma such as visual acuity, vertical cup disc ratio and visual field defects were not associated with depression (Wang ST et al, 2012; Skalicky S et al, 2007; Jampel HD et al, 2007). This indicates that glaucoma patients perception of the disease plays a role and it is important to counsel and allay fears of the disease.

In a cross sectional study, significant predictors of depression after adjustment for demographic and systemic disease variables included difficulty performing close work ($p=0.005$), difficulty with steps ($p<0.001$), difficulty with side vision ($p=0.001$) and difficulty driving during the daytime ($p=0.004$) (Wang SY et al, 2012). Another cross sectional study found that depression was associated with dependency

($p<0.001$), difficulty performing vision specific roles such as driving, housework, walking ($p=0.015$) and distance vision activites ($p=0.013$) (Owsley C, 2004).

Depression significantly reduces one's ability to adhere to treatment (Sleath B et al, 2006; Pappa C et al, 2006; Wing RR et al; 2002). This was compounded by the fact that elderly glaucoma patients have cognitive impairment resulting in impaired memory (Stryker et al, 2010; Sleath B et al, 2006; Hagerman KE et al; 2007). Problems with adherence is possibly due to the lost of hope for vision recovery, side effects of treatment or lose of initiative to make the effort to adhere to treatment.

It has been found that depression levels of glaucoma patients decreased over time after the initial diagnosis (Zhou C et al, 2013; Janz NK et al, 2006; Wilson MR et al, 2002). This is due to the initial fear of blindness and worry at learning of the diagnosis; which reduces over time from reassuarance, regular follow up, acceptance and more knowledge (Janz NK et al, 2006; Odberg et al, 2001). Age was also associated with fear of blindness with younger patients reporting more fear of blindness at onset (Janz NK et al, 2001, Odberg et al, 2011). This is due because youger patients have more years of living with diagnosis therfore anticipating more adverse outcomes (Janz NK et al, 2001, Odberg et al, 2011).

1.4.3 GERIATRIC DEPRESSION SCALE

There are numerous depression scales that have been developed such as Zung Rating Scale, Hamilton depression scale and Becks Depression Inventory (Hamilton M,

1960; Zung WWK, 1965; Beck AT, 1996). However, these depression rating scales have been developed and validated for the use of a younger population with many questions measuring somatic complaints. Its applicability with older individuals are limited as elderly population have multiple existing medical problems and the use may elevate the scores of non depressed older persons (Yesavage JA & Brink TL, 1981; Heo M et al, 2007). Furthermore, the depression scales have not been validated for the use in the elderly population (Hamilton M, 1960; Zung WWK, 1965; Carroll et al, 1973).

The Geriatric Depression Scale (GDS) was developed with the recognition that depressive symptoms in elderly patients require a questionnaire that is able to discriminate depressive symptoms from the general characteristics of the elderly population. It focuses instead on the psychosocial aspects of depression. GDS was created initially as a 30 item questionnaire (Yesavage JA & Brink TL, 1981). It can be self administered or presented as an interview. It consists of a yes/no format to make the scale simple and easily understood by the elderly (Yesavage JA & Brink TL, 1981). GDS has a sensitivity of 92% and a specificity of 89%. (Koenig HG et al, 1998). A shorter version consisting of 15 items was later created to ease the process as it takes 5-7 minutes to complete (Sheik J & Yesavage JA, 1986). The shorter version was highly correlative to the long version ($r = 0.84$) (Herrman N et al, 1996; Lesher EL, 1994).

In patients with cognitive impairment, 2 studies found that the GDS score was valid for elderly with scores above 15 out of 30 on a Mini Mental State Examination (MMSE) (Jongenelis K et al, 2005; McGivney SA, 1994). However, Gerritsen et al

(2007) noted that GDS was valid for MMSE scores of 5 or more suggesting that only severely demented patients were not able to complete GDS. This finding was echoed by Conradsson M et al (2013) where GDS was found to be valid for MMSE score of 10 or more. Therefore administration of GDS in cognitive impaired patients should be done with their caregiver. Some studies have demonstrated that the Geriatric Depression Scale is able to detect depression better than medical and nursing staffs (Rapp et al, 1988; Jackson R & Baldwin B, 1993).

1.4.4 MALAY VERSION-GERIATRIC DEPRESSION SCALE-14 (mGDS 14)

The shorter English version GDS consisting of 15 questions was translated and validated in the Malay language in 2004 by Teh EE et al (2004) to be used in local elderly population. mGDS 14 was translated and validated, leaving out question 9 (preference of living at home rather than going out) as most elderly in the local culture are relatively introvert and emphasis is on family rather than individual lifestyle (Teh EE & Hasanah CI, 2004). Therefore, most patients gave a positive response to question 9 despite their depressive state. The final questionnaire contained 14 questions which makes it easy to be adminitered in the elderly patients.

Patients with the score of 8 and above are considered depressed (Teh EE & Hasanah CI, 2004). The mGDS 14 has satisfactory correlation with depression as a screening scale for depressed elderly patients when the score of mGDS 14 was compared to the clinical diagnosis of depression (Teh EE & Hasanah CI, 2004).